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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,748	10/27/2005	Alejandro Merino	085449-0159	6988

22428 7590 07/09/2008

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EXAMINER	
LEE, JAE W	

ART UNIT	PAPER NUMBER
1656	

NOTIFICATION DATE	DELIVERY MODE
07/09/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Office Action Summary	Application No.	Applicant(s)	
	10/521,748	MERINO ET AL.	
	Examiner	Art Unit	
	JAE W. LEE	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application status

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/16/2008 has been entered.

In response to the previous Office action, an advisory action (mailed on 03/17/2008), Applicants filed a response and amendment received on 04/16/2008. Said amendment canceled Claims 1-48, 55 and 56, and amended Claims 49, 51 and 54. Thus, Claims 49-54 are at issue and present for examination.

Applicants' arguments filed on 04/16/2008, have been fully considered, and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Objections to the Oath or Declaration

The Examiner acknowledges that Applicants are currently in the process of preparing a supplemental declaration to be submitted.

Claim Objections

The previous objection of Claim 49 for the recitation of "KDA" is withdrawn because Applicants have deleted "KDA."

Claims 49-54 are objected to because of the following informalities:

Claim 49 is objected to because the recitation of "complex comprising SEQ ID NO: 10 and SEQ ID NO: 15" can be improved with respect to form. The Examiner suggests replacing the noted phrase with ---complex comprising the amino acid sequences of SEQ ID NO: 10 and SEQ ID NO: 15---.

Claims 49 and 51 are objected to because the recitation of "one or more candidate molecules" can be improved with respect to form. The Examiner suggests replacing the noted phrase with ---a candidate molecule---.

Claims 50 and 53 are objected to because the recitation of "a molecule" can be improved with respect to consistency. The Examiner suggests replacing the noted phrase with ---a candidate molecule---.

Claim 52 is objected to because the recitation of "a drug" can be improved with respect to consistency. The Examiner suggests replacing the noted phrase with ---a candidate molecule---.

Claim 54 is objected to because the recitation of "an identified molecule" can be improved with respect to consistency. The Examiner suggests replacing the noted phrase with ---an identified candidate molecule---.

Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 49-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 49 (50-54 dependent therefrom) recites the phrase "determining whether beta amyloid precursor protein processing of a substrate to the complex is modified in the presence of the one or more candidate molecules" in step (c), which is unclear and indefinite. It is confusing because there is a discrepancy between this step (c) and the preamble. [1] Determining the modification of beta amyloid precursor protein processing of a substrate to the complex, as recited in step (c), and [2] a method for screening for a candidate molecule that modify beta-amyloid precursor protein processing by binding to a protein complex comprising SEQ ID NO: 10 and SEQ ID NO: 15, as recited in the preamble, are two completely different thing. As such step (c) has very little to do with what the claimed method is intended for.

Claim 50 (53 and 54 dependent therefrom) is unclear and indefinite with respect to how it further limits claim 49, since claim 49 is directed to a different intended use than that of claim 50. As such, it is unclear how claim 50 is drawn to methods having a broader scope than claim 49 because methods of claim 50 not only encompasses a method for screening for molecules that modify processing of APP, but also a method for screening for a molecule that modulates function, activity, composition, or formation of a complex comprising SEQ ID NO:10 and 15. In addition, it is unclear how the methods of claim 49 can be used for "screening for a molecule that modulates directly or indirectly the function, activity, composition, or formation of the complex," as recited in claim 50, without a step of determining whether there is a modulation of function, activity, composition, or formation of the complex. If the intended limitation is a method of claim 49, wherein the molecule that binds the complex also modulates function, activity, composition, or formation of the complex, the claim should be amended to recite, for example, "the method of claim 49, wherein the candidate molecule that binds to the complex modulates directly or indirectly the function, activity, composition or formation of the complex."

Claim 51 recites the phrase, "(a) isolating the complex from the cell or organism to produce an isolated complex or protein component," which is unclear and indefinite. It is confusing and unclear with regard to how one can isolate the complex from the cell or organism in order to produce an isolated complex or protein component. If the intended limitation is the isolation of the complex from the cell or organism prior to exposing the complex to the candidate molecule, it is suggested the claim be amended

to recite, for example, "the method of claim 49, wherein the method further comprises isolating the complex from the cell or organism prior to exposing the complex to the molecule".

Claim 51 recites the phrase "(c) determining whether processing of the substrate is modified in the presence of the one or more candidate molecules," which is unclear and indefinite. It is confusing because there is a discrepancy between this step (c) and the preamble of claim 49. [1] determining whether processing of the substrate is modified in the presence of the one or more candidate molecules as recited in claim 51 (c), and [2] a method for screening for a candidate molecule that modify beta-amyloid precursor protein processing by binding to a protein complex comprising SEQ ID NO: 10 and SEQ ID NO: 15, as recited in the preamble, are two completely different things. As such step (c) has very little to do with what the claimed method is intended for.

Claim 51 recites the phrase "protein component," which is unclear and indefinite. It is unclear with respect to what the phrase encompasses. For example, does the protein component encompasses only peptides" Or does it also encompasses secondary, tertiary or quaternary structures of proteins. Alternatively, does the phrase mean a part/fragment of the complex as recited in claim 49? It is noted by the Examiner that if the "protein component" is a fragment of the complex recited in claim 49, there is lack of antecedent basis for the noted phrase in claim 49, because the complex must comprise both SEQ ID NOs: 10 and 15 in their entirety.

Claim 52 indicates that the method of claim 49 is intended for "screening for a drug useful in treating or preventing a disease or disorder such as neurodegenerative

diseases such as Alzheimer's disease." However, it is unclear and indefinite because the method of claim 49, which is drawn to a method of determining whether a candidate molecule binds to the complex, lacks any additional steps necessary for determining whether the drug is useful in treating or preventing a disease. Claim 49 only requires determining whether binding occurs between a complex and a candidate molecule, which is not enough to determine if the candidate molecule that binds to the complex is useful in treating/preventing a disease.

Regarding claim 52, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 53 indicates that the method of claim 50 is intended for "screening a molecule that modulates the apoptotic activity of the complex." However, it is unclear and indefinite because claim 49, from which claim 53 ultimately depends, is drawn to a method of determining whether a candidate molecule binds to the complex. If the intended limitation is, the method of claim 50, wherein the activity modulated by the candidate molecule is the apoptotic activity of the complex, it is suggested the claim be amended to recite, for example, "the method of claim 50, wherein the candidate molecule that binds to the complex also modulates the apoptotic activity of the complex."

Claim 54 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is a step of identifying a candidate

molecule as a therapeutic agent before one adds the pharmaceutically acceptable carrier.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The previous rejection of Claims 49-54 under 35 U.S.C. § 112, first paragraph, written description, as failing to comply with the written description requirement, is withdrawn by virtue of Applicants' amendment because claims have been amended so that they are limited to the use of SEQ ID NOs: 10 and 15 in the claimed methods. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The previous rejection of Claims 49-54 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is withdrawn by virtue of Applicants' amendment because claims have been amended sot that the scope of the claimed methods are limited to the use of SEQ ID NOs: 10 and 15.

Claims 49-54 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for [1] a method for

screening for a candidate molecule that modifies beta-amyloid precursor protein processing, wherein said method requires determining whether the candidate molecule binds to a complex comprising SEQ ID NO: 10 and SEQ ID NO: 15, and wherein said complex is recombinantly produced by isolated host cells, and [2] a method for screening for a candidate molecule wherein said candidate molecule can potentially be useful in treating or preventing a disease or disorder, does not reasonably provide enablement for [1] a method for screening for a candidate molecule that modifies beta-amyloid precursor protein processing, wherein said method requires determining whether the candidate molecule binds to a complex comprising SEQ ID NO: 10 and SEQ ID NO: 15, and wherein said complex is recombinantly produced by non-isolated host cells or multicellular organisms, and [2] a method for screening for a candidate molecule wherein said candidate molecule is useful in treating or preventing any disease or disorder, as recited in claim 52. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 49-54 are drawn to a method for screening for a one or more candidate molecules that modify beta-amyloid precursor protein processing by binding to a protein complex comprising SEQ ID NO: 10 and SEQ ID NO: 15, said method comprising the steps of: (a) exposing the complex comprising SEQ ID NO: 10 and SEQ ID NO: 15, or a cell or organism expressing the complex, *which include making and using transgenic cell/organism expressing the complex*, to the one or more candidate molecules; (b) determining whether the one or more candidate molecules is/are bound to the complex;

and (c) determining whether beta-amyloid precursor protein processing of a substrate to the complex is modified in the presence of the one or more candidate molecules. Claim 52 further requires screening for a drug useful in treating or preventing any disease. See Claim Rejections under 35 USC 112, second paragraph, for claim interpretation.

Nature Of Invention:

The instant invention is related a method which requires making and using transgenic cell/organism expressing the complex comprising SEQ ID NO: 10 and SEQ ID NO: 15, as well as a method which requires testing to determine whether a compound is useful in treating or preventing any disease.

Breadth Of Claims And Guidance Provided By The Inventor:

The scope of invention as claimed encompasses making and using any transgenic cell/organism expressing the complex comprising SEQ ID NO: 10 and SEQ ID NO: 15. The scope of the invention of claim 52 further requires any number of unknown steps to determine whether a drug is useful in treating or preventing any disease.

The specification fails to disclose a single method of making and using a transgenic organism expressing the complex comprising SEQ ID NO: 10 and SEQ ID NO: 1, which could be used to screen candidate molecules that bind to said complex. Applicants' disclosure with respect to making and using transgenic organism is briefly noted in the embodiment section on page 102, last paragraph, wherein Applicants note that transgenic non-human animals can be used in the claimed methods. However,

since the specification fails to provide adequate guidance with respect to making and using a particular transgenic organism expressing the complex comprising SEQ ID NO: 10 and SEQ ID NO: 1, it would require an extensive and undue amount of experimentation to practice the invention as claimed, especially in view of the fact that making transgenic organisms across the entire animal kingdom is considered highly unpredictable. In addition, the specification is completely silent as to the additional steps required in any method for screening for a drug that is used in treating or preventing any disease. It is noted that to screen for a drug useful in treating or preventing a disease, one of skill in the art would have to determine not only if the drug binds to a complex comprising SEQ ID NO: 10 and 15 and modifies processing of the beta-amyloid precursor protein, but also whether those drugs which bind to the complex and modify the processing of the beta-amyloid precursor protein prevent or treat a disease. One of skill in the art would not reasonably expect all molecules that bind to the complex and modify processing of beta-amyloid precursor protein to be useful in treating or preventing any disease due to the many complex interactions found *in vivo* which could affect the ability of a compound to bind the complex and modify beta-amyloid precursor protein processing. Therefore, a method for screening for compounds that treat or prevent a disease will require any number of steps including testing in human subjects (e.g., clinical trials) such that one could determine whether a particular drug is useful in treating or preventing any disease. It is also important to note that the specification is silent with regard to the structural features found in any compound that binds to the complex and modifies processing of the beta-amyloid precursor protein that

would allow one of skill in the art to determine *a priori* whether the compound can be used to treat or prevent a disease, or which diseases/disorders can be treated with said compound.

State Of Art And Predictability:

The state of transgenic art at the time of filing was such that phenotype of an organism is determined by a complex interaction of genetics and environment. The phenotype examined in a transgenic and knock out model is influenced by genetic background, which is the collection of all genes present in an organism that influence a trait or traits. The genes may be part of same biochemical or signaling pathway or of an opposing pathway or may appear unrelated to the gene being studied. Furthermore, allelic variations and the interactions between the allelic variants also influence a particular phenotype. These effects can dramatically alter the observed phenotype and therefore can influence or later the conclusions drawn form the transgenic or knockout models

Furthermore, the transgene expression and physiological consequences of transgene products in non-mouse mammals are not always accurately predicted among various species of mammals. The lack of understanding of essential genetic control elements make it difficult to predict the behavior of any transgene in any organism because the transgene expression is influenced by position effect in transgenic organisms. The individual gene of interest, promoter, enhancer, coding or non-coding sequences present in the transgene construct and the site of integration, are the

important factors that govern the expression of a transgene. The cis acting elements of one species may interact with different transactivating factors in other species. For example, the introduction of human growth hormone transgene in mice results in mammoth mouse phenotype, where as expression of the same transgene in pig results in premature death of transgenic pigs. Furthermore, many biochemical pathways are plastic in nature, which reflects the ability of the embryo to use alternative gene when the preferred gene is modified. It is known in the art that the level and the specificity of a transgene as well as the phenotype of the transgenic organism are greatly dependent upon the specific expression vector used. The individual gene of interest, promoter, enhancer, coding or non-coding sequences present in the transgene construct and the site of integration, for example are the important factors that govern the expression of a transgene.

In addition, multicellular organisms are the current evolutionary summation of more than one billion years of selection. Their complexity means that even a humble mouse cannot be used as a simple tool. For example, extensive phenotype tests even in mice have shown that abnormal phenotypes were sometimes detected in physiological areas where they were not initially anticipated, or only manifested under certain conditions, emphasizing the need for careful phenotypic investigation. Nevertheless, the effect of some genes became evident only upon inactivation of another gene, pointing to the phenomenon of biological robustness. Therefore considering the scope of invention as claimed, at issue, under the enablement requirement of 35 U.S.C. 1 12, first paragraph is whether, given the Wands-factors, the

experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See Fields v. Conover, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970). The state of the transgenic art clearly concludes that poor embryo survival, low transgene integration rate and unpredictable transgene behavior are the three primary contributors that determines that fate of a transgenic organism made. *see Taft et al Trends in Genetics 22(12):649-653, 2006; Linder, Lab. Anim. 30(5):34-39, 2001; Bilbo et al, Lab. Anim. 30(1):24-29, 2001; Holschneider et al, Int. J. Dev. Neuroscience 18 :615-618, 2000; Wood. Comp. Med. 50(1): 12-15, 2000; Sigmund, Arterioscler. Throm. Vasc. Biol. 20:1425-1429, 2000; Kappel et al. Current Opinion in Biotechnology 3:558-553 1992.*

With regard to Claim 52, the art teaches the unpredictability of determining whether a compound which appears to be promising for treating or preventing a disease can in fact be useful in treating or preventing a disease/disorder without carrying out a significant amount of experimentation in non-human and human subjects. Currently, the determination as to whether a compound is useful for treatment or prevention of a disease requires a vast amount of experimentation, which includes clinical trials, to determine not only if the compound is safe but also if it has the desired effect on a human subject. The art is replete with reports disclosing the extensive amount of research and testing required to determine whether drugs which appear to be good

candidates to treat or prevent a disease are drugs which can be used to treat or prevent a disease.

Taken together, any method of making and using all transgenic cells/organisms, and methods which require an extensive amount of testing to determine whether a compound is useful in preventing or treating a disease as claimed are not considered routine in the art and without sufficient guidance to make and use the claimed invention, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Claim Rejections - 35 U.S.C. § 102

The previous rejection of Claims 49-54 under 35 U.S.C. § 102(b) as being anticipated by Underhill et al. (A Novel Nuclear Receptor Corepressor Complex, N-CoR, Contains Components of the Mammalian SWI/SNF Complex and the Corepressor KAP-1, J. Biol. Chem., Vol. 275, Issue 51, 40463-40470, December 22, 2000), is withdrawn by Applicants' amendment because Underhill et al. do not teach a method of using SEQ ID NOs: 10 and 15 to determine whether beta-amyloid precursor protein processing of a

substrate to the complex is modified in the presence of the one or more candidate molecules.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 49-54 are rejected under 35 U.S.C. 102(a) as being anticipated by Kohishita et al. (The gamma Secretase-generated Carboxyl-terminal Domain of the Amyloid Precursor Protein Induces Apoptosis via Tip60 in H4 Cells, Journal of Biological Chemistry, Vol. 277, No. 32, pp. 28530–28536, published online on 05/14/2002).

Claims 49-54 are drawn to a method for screening for a one or more candidate molecules that modify beta-amyloid precursor protein processing by binding to a protein complex comprising SEQ ID NO: 10 and SEQ ID NO: 15, said method comprising the steps of: (a) exposing the complex comprising SEQ ID NO: 10 and SEQ ID NO: 15, or a cell or organism expressing the complex, to the one or more candidate molecules; (b) determining whether the one or more candidate molecules is/are bound to the complex; and (c) determining whether beta-amyloid precursor protein processing of a substrate to the complex is modified in the presence of the one or more candidate molecules; optionally isolating and contacting said complex or protein component, and/or mixing said candidate molecule with a pharmaceutically acceptable carrier, and other "intended

uses" for the method of claim 49 as recited in claims 50, 52 and 53. See Claim Rejections under 35 USC 112, second paragraph for claim interpretation.

Kinoshita et al. teach a method comprising the steps of: (a) exposing the Tip60 complex comprising HDAC1 (SEQ ID NO: 10) and SWI/SNF complex 60 kDa subunit (SEQ ID NO: 15, or also known as SMARDCD2, baf60b, rsc6b or pro2451), or the H4 cells, derived from human neuroglioma cells, expressing the Tip60 complex, to the one or more candidate molecules, i.e., APP-C58-Myc (amyloid precursor protein mutant) labeled with Cy3; (b) determining whether the APP-C58-Myc is bound to the Tip60 complex labeled with fluorescein via FRET (see pg. 28530-1 under Material and Methods; and Figure 4 A-D). Because the expression of APP-C58-Myc in H4 cells leads to apoptosis and cell death via its interaction with Tip60 complex (see Figure 2), the methods taught by Kinoshita effectively determines whether beta-amyloid precursor protein processing of a substrate to the complex is modified in the presence of the APP-C58-Myc. It is noted by the Examiner that Tip60 complex taught by Kinoshita et al. inherently comprises proteins listed in Tables 1 and 2 of the specification which include HDAC1 (SEQ ID NO: 10) and SWI/SNF complex 60 kDa subunit (SEQ ID NO: 15). It is further noted by the Examiner that the "intended use" of claimed methods as recited in claim 52, i.e., "for screening for a drug useful in treating or preventing a disease such as neurodegenerative diseases such as Alzheimer's disease," is given a limited patentable weight. Claim 54 is included in this rejection because the methods taught by Kinoshita et al., comprise mixing an identified molecule, i.e., APP-C58-Myc labeled with Cy3, with a pharmaceutically acceptable carrier, i.e., Tris-buffered saline (see pg. 28531, left

column, under "Immunohistochemistry"). Therefore, claims 49-54 are anticipated by the reference of Kinoshita et al.

Conclusion

Claims 49-54 are rejected for the reasons as stated above. Applicants must respond to the objections/rejections in this Office action to be fully responsive in prosecution.

This office action is non-final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jae W. Lee whose telephone number is 571-272-9949. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen K. Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JAE W LEE/

Examiner, Art Unit 1656

/Delia M. Ramirez/

Delia M. Ramirez, Ph.D.
Primary Examiner – Art Unit 1652